PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference A158134	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/IB 03/05673	International filing date *(day/month/year)* 01.12.2003	Priority date *(day/month/year)* 05.12.2002
International Patent Classification (IPC) or both national classification and IPC A61K31/202		
Applicant PROYECTO EMPRESARIAL BRUDY, S.L.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 1-2 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
27.05.2004	21.03.2005
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Stoltner, A Telephone No. +49 89 2399-8408

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/IB 03/05673

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-9 as originally filed

Claims, Numbers

1-14 received on 03.12.2004 with letter of 02.12.2004

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-14
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-14
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-14
	No:	Claims	

2. Citations and explanations

see separate sheet

1). Claim 1 as presently on file, concerns the use of extract of animal/plant/microbial origin comprising docosahexaenoic acid (DHA) for the treatment of lipodystrophy in a mammal, **said medicament being administered to a patient who is concomitantly receiving a highly active anti-retroviral therapy (HAART).**

1a) The amendments carried out to claim 1 find basis in the originally filed application (cf. page 5, lines 14-31) and therefore meet the requirements of Art. 34(2)(b) of the PCT.

2a) As to the definition of "lipodystrophy", according to the definitions in page 2, lines 8-18, this term encompasses a multifactorial illness wherein not only the metabolism of fatty acids is involved, but also the metabolism of glucids, etc.. This is evident from the the scientific documents denoted as enclosures 1 and 2 provided by the Applicant in his letter of reply.

2b) On the other hand, the problem to be solved lies in the provision of a treatment of lipodistrophy whithout toxic side effects caused to HIV infected patients having developed lipodistrophy during their HAART treatment.

2c) As such, the cited prior art documents will be reconsidered with respect to the subject-matter of the present application:

D1, Prostaglandins, Leukotrienes and Essential Fatty Acids, 37(2), aug. 1989, pp. 135-137, Bégin M.E. et al., report that polyunsaturated fatty acids (PUFA) modulate the immune system and inactivate viruses in-vitro. Moreover, D1 stresses the reduced levels on C20 and C22 essential fatty acids including DHA in a significant and selective way in patients infected with the aids virus (cf. abstract, page 136, 2nd para., page 137, table 4, and 2nd para. on the left-sided col.). The supplemental addition of n-3 PUFA (implitly including **DHA**) as **nutritional support** is strongly recommended in D1 (cf. page 137, 2nd col.).

D2, FR-A-2 749 133, provides **nutritional supplements containing DHA** for improving lipid metabolism in aids patients (cf. abstract, page 1, lines 5-15, page 13, lines 34-40, claim 11).

D3, DE-A-40 17 979, provides a lipid mixture used as medicine and for **dietary nutrition**, containing DHA for treating diseases associated with lipid coated viruses with particular reference to HIV-1 infections (cf. abstract, examples 1-3).

D4, EP-A-378 824, discloses the use of omega-3-fatty acids in the treatment of patients suffering from cachexia caused by tumors or due to aids infection (cf. abstract, page 2, 1st para., claims 1-3).

3). As none of the documents cited above discloses or even suggests the use of DHA in the treatment of lipodystrophy in a patient receiving concomitantly a high active anti-retroviral therapy (HAART), the use as presently intended has to be acknowledge both novel and inventive pursuant to Arts. 33(2) and 33(3) of the PCT.

ENCLOSURE-1

CLAIMS

<(*)> <said medicament being administered to a patient who is concomitantly receiving a highly active anti-retroviral therapy (HAART)>

1. Use of an extract of animal, plant or microorganism-produced origin that comprises docosahexaenoic acid as active substance for the manufacture of a medicament for the treatment of lipodystrophy in a mammal <(*)>

2. Use according to Claim 1, characterised in that the amount of docosahexaenoic acid in said extract is higher than or equal to 100 mg/day.

3. Use according to Claim 2, characterised in that said amount of docosahexaenoic acid in said extract is 4 grams/day.

4. Use according to any of claims 1 to 3, in which the medicament promotes adipocytary differentiation.

5. Use according to any of claims 1 to 3, in which the medicament has hypolipemiant activity.

6. Use according to any of claims 1 to 3, in which the medicament reduces the alpha tumour necrosis factor.

7. Use according to any of claims 1 to 3, in which the medicament has antihypertensive activity.

8. Use according to claim 1, in which the medicament is capable of inhibiting the toxic effects caused by the administration of an antiretroviral drug.

9. Use according to Claim 1, in which said docosahexaenoic acid is present in said extract in a concentration which ranges between 5% and 100% (w/w).

10. Use according to Claim 9, in which said docosahexaenoic acid is present in said extract in a concentration which ranges between 50% and 100% (w/w).

11. Use according to any of the preceding claims, in which the medicament is administered orally.

12. Use according to any of the preceding claims, in which the drug is administered parenterally.

13. Use according to Claim 1, in which said mammal is a human.

14. Use according to Claim 13, in which said human is infected with the HIV virus.